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# **Sensory feedback signal derivation from afferent neurons**

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## **QUARTERLY PROGRESS REPORT #3**

for the period

**1 June 1993 -- 31 August 1993**

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## I Summary of the Overall Project

In this study we are exploring the feasibility of extracting 1) cutaneous sensory information about fingertip contact and slip, and 2) proprioceptive sensory information about wrist or finger position. We use implanted nerve cuff electrodes to record peripheral nerve activity in animal models.

Our overall **objectives** for the 3-year duration of this contract are as follows:

1. Investigate, in cadaver material, implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded.
2. Select a suitable animal preparation in which human nerve dimensions and electrode placement sites can be modeled and tested, with eventual human prosthetic applications in mind.
3. Fabricate nerve cuff electrodes suitable for these purposes, and subcontract the fabrication of nerve cuff electrodes of an alternate design.
4. Investigate the extraction of information about contact and slip from chronically recorded nerve activity using these animal models and electrodes. Specifically,
  - a. Devise recording, processing and detection methods to detect contact and slip from recorded neural activity in a restrained animal;
  - b. Modify these methods as needed to function in an unrestrained animal and in the presence of functional electrical stimulation (FES);
  - c. Record activity for at least 6 months and track changes in neural responses over this time.
5. Supply material for histopathological examination from cuffed nerves and contralateral controls, from chronically implanted animals.
6. Investigate the possibility of extracting information about muscle force and limb position from chronically recorded neural activity.
7. Cooperate with other investigators of the Neural Prosthesis Program by collaboration and sharing of experimental findings.

## II. Summary of our Progress *Prior to the Third Quarter*

**In the first quarter** we completed objective 1 and made progress toward objectives 2 and 3. In three human cadaver arms, we found appropriate implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded. We selected the cat forelimb as the animal preparation in which human nerve dimensions and electrode placement sites are being modeled and tested. We investigated the details of the innervation of the paw and the forelimb musculature in three cats, identified several possible implantation sites, and started to design cuff electrodes suitable for these purposes.

**In the second quarter** we built 38 nerve cuff electrodes in assorted sizes, suitable for implantation on four nerves in the left forelimb of cats: the proximal median nerve, proximal ulnar nerve, distal median nerve, and distal ulnar nerve (objective 3). We implanted four cuffs in each of three cats, and began to follow the cuff impedance and compound action potential (CAP) properties periodically (objective 4c). We also started to design a forelimb reaching task and the hardware required to extract information about contact and slip from chronically recorded nerve activity (objective 4a, 4b).

### III. Summary of Progress in the Third Quarter

In the third quarter we built 22 additional nerve cuffs, completing objective 3 for Year 1. We implanted four cuffs in each of 5 additional cats, completing a series of 8 cats implanted in the first year. We continued to monitor cuff impedance and compound action potential (CAP) properties periodically (objective 4c) in all 8 cats. We refined the design of the forelimb reaching task, and started the hardware design (objective 4a,b). We started to obtain the equipment required for in-house histopathological examination of cuffed nerves and contralateral control nerves (objective 5).

### IV. Details of Progress in the Third Quarter

#### A. Characteristics of Nerve Cuff Electrodes

In the third quarter we completed the series of 8 implantations scheduled for the first year. In all 8 cats we used "conventional" cuffs built in the laboratory, as described in Progress Report #2 and, e.g., Hoffer (1990)<sup>1</sup>. Nerve sizes and dimensions of cuffs used are summarized in Table 1.

TABLE 1. Nerve dimensions and dimensions of cuffs used in 8 cats (Year 1)

Nerve dimension Cuff dimension	NIH 1	NIH 2	NIH 3	NIH 4	NIH 5	NIH 6	NIH 7	NIH 8
Distal Ulnar (Palmar)	1*2 * 20 1.6 * 15	1.5 * 15 2.0 * 15	1*2 * 18 2.0 * 15	2.5 * 19 2.5 * 15	1.5 * 18 2.0 * 15	1.0 * 19 2.0 * 15	1.8 * 21 2.0 * 15	1.0x1.7 * 20 1.6 * 15
Distal Median	1.5 * 14 1.6 * 15	1.75 * 15 2.0 * 15	1.5 * 18 2.0 * 15	1.5 * 25 2.0 * 15	1.5 * 20 2.5 * 15	1.0 * 23 1.6 * 15	1.7 * 28 2.0 * 15	1.0 * 20 1.6 * 15
Proximal Ulnar	2.0 * 15 2.5 * 15	----- 2.5 * 10	1.5*2.5*20 2.6 * 15	2.5 * 19 2.8 * 15	2.0 * 19 2.5 * 15	2.0 * 17 2.5 * 15	2.0 * 19 2.5 * 15	2.0 * 18 2.5 * 10
Proximal Median	2.0 * 10 2.5 * 10	----- 2.5 * 5	2.0 * 14 2.5 * 10	2.2 * 21 2.5 * 15	2.5 * 15 2.5 * 15	1.8 * 18 2.0 * 15	2.0 * 16 2.5 * 15	1.5 * 18 2.0 * 15

Nerve dimensions (diameter \* free length) on top; cuff dimensions (inside diameter \* length) below.

'-----' signifies data not recorded Nerve diameter of n\*n signifies a ribbon-shaped nerve.

All dimensions in mm.

A total of 61 cuffs of assorted sizes were built, of which 33 were implanted (one implanted cuff was replaced subsequently). The distribution of cuff dimensions is summarized in table 2.

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1. Hoffer, J.A. Techniques to record spinal cord, peripheral nerve and muscle activity in freely moving animals. In: *Neurophysiological Techniques: Applications to Neural Systems. Neuromethods 15*, A. A. Boulton, G.B. Baker and C.H. Vanderwolf, Eds. Humana Press, Clifton, N.J., p.65-145, 1990.

TABLE 2. Summary of cuff sizes used in Year 1 (8 cats \* 4 nerves)

Cuff Inside Diameter	Cuff Length		
	5 mm	10 mm	15 mm
1.6 mm	-----	-----	5
2.0 mm	-----	-----	11
2.5 mm	1	4	9
2.6 mm	-----	-----	1
2.8 mm	-----	-----	1

## B. Surgical Protocol

**Anesthesia:** Induction: Ketamine Hydrochloride (5mg/kg) and Valium (Diazepam) (0.2mg/kg) were given intravenously in the right cephalic vein. Maintenance: after an infant intra-tracheal catheter was installed, surgical level of anesthesia was maintained with 0.5 - 1.5% Halothane in oxygen. Rectal temperature, EKG, expired CO<sub>2</sub>, breathing rate and reflexes were monitored.

**Surgical preparation:** Three areas were shaved: neck, back, and left forelimb from shoulder to wrist (see Fig. 1). The backpack connector location was marked.

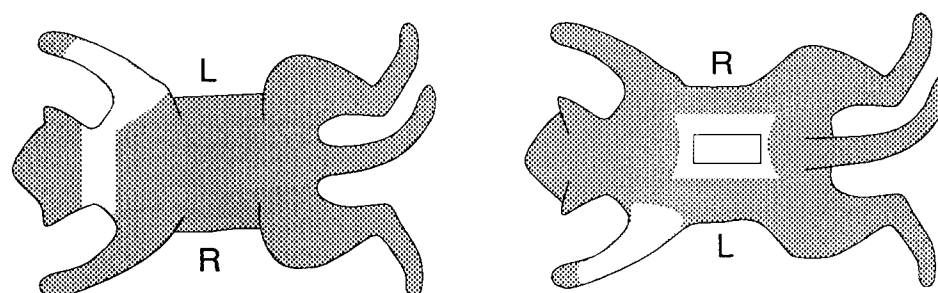


Fig. 1: Shaving areas. Neck, back and left forelimb. The rectangle indicates the outline of the backpack.

**Backpack installation:** A PC board with a 40 pin connector was used as a backpack interface. The board edges were padded with silicone tubing. The backpack was anchored by passing two #2 Mersilene sutures around the L1- L2 and L4 - L5 dorsal intervertebral ligaments.

**Jugular catheter:** For permanent intravenous access, a jugular catheter was implanted in a superficial jugular vein. The catheter was made of silicone tubing (Dow corning 602-205), and was inserted 3.5-4 cm in the vein and coursed 30-50 cm subcutaneously to an access port in the backpack (Hoffer, 1990). The catheter is kept filled with a 4% Heparin solution to avoid blockage.

**Tripolar nerve cuffs:** A total of four tripolar cuffs were implanted on the Median and Ulnar nerves in the left forelimb, as shown in Fig. 2. The exact location for the installation of each cuff depended on the local branching patterns of minor blood vessels and fine nerve branches. Two incisions were made, one above and one below the elbow.

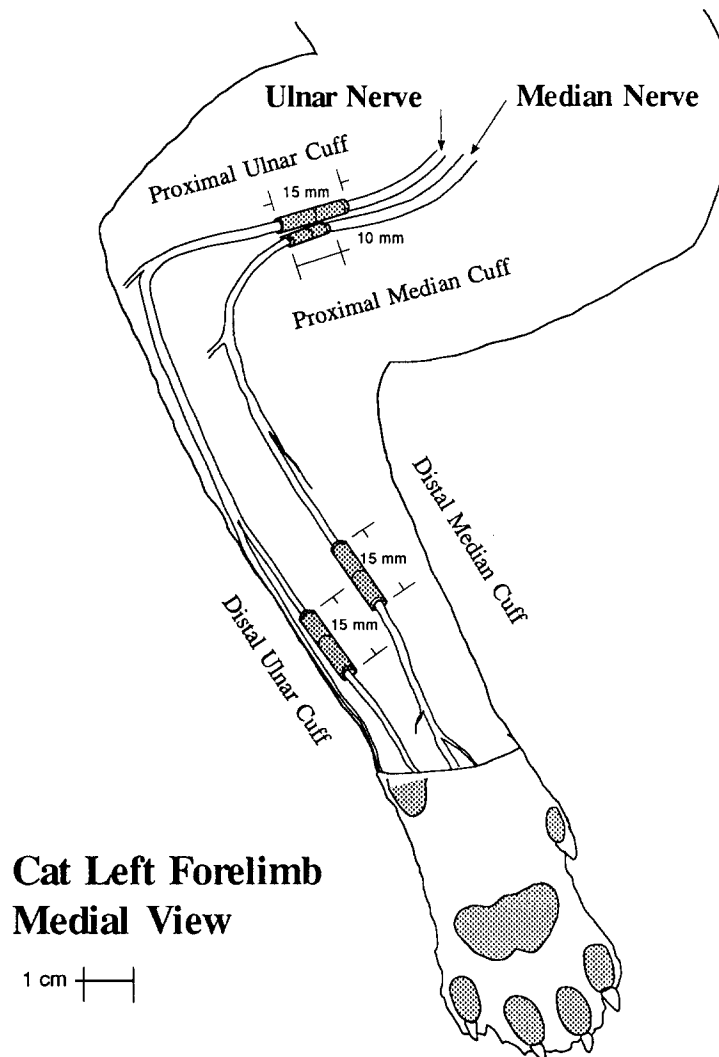
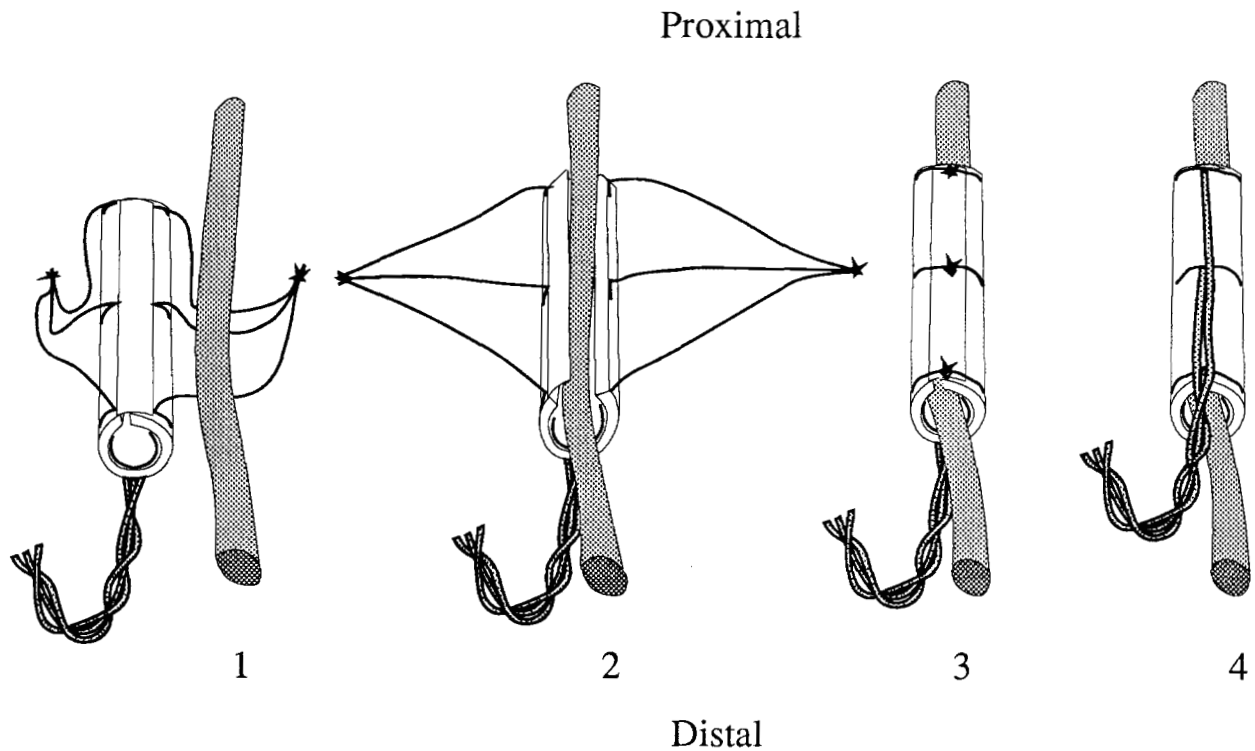


Fig. 2: Locations of nerve cuffs.

**Distal nerve branches:** A 6-7 cm medial incision was made along the middle of Palmaris Longus (Pal L) starting 1-2 cm proximal to the wrist. After blunt dissection of the superficial fascial layers overlying the Pal L muscle, the tendinous antebrachial fascia was opened. Blunt dissection between Pal L and Flexor Carpi Ulnaris (FCU) gained access dorsally to the Ulnar nerve (Palmar branch), and between Pal L and Flexor Carpi Radialis (FCR) gained access ventrally to the Median nerve. Both nerves were carefully freed from connective attachments for 17-20 mm. If the Ulnar Palmar branch could not be separated from the Ulnar Dorsal Cutaneous branch, then a larger cuff was placed around both nerves. Each cuff was installed by passing the three sutures under the nerve, placing the opening of the cuff just under the nerve, as shown in Fig. 3 (part 1). By pulling the sutures apart, the cuff opened and the nerve dropped in (Fig. 3, part 2). The cuff was closed by tying the three sutures (Fig. 3, part 3) and was then rotated so the leadout wires were on top (Fig. 3, part 4). The lead wires exited the cuff in the distal direction and made a wide loop to turn in the proximal direction, thus providing strain relief.



**Fig. 3: Installation of cuff.** 1) Cuff sutures passed under the nerve. 2) Cuff opened for nerve to slip in. 3) Cuff closed by tying the three sutures. 4) Cuff rotated into final position.

**Proximal nerve branches:** A 5-7 cm incision was made medially above the elbow, parallel to the humerus bone. To reach the Median and Ulnar nerves, the Pectoralis, Pectoantibrachialis and/or Epitrochlearis muscles must be reflected. It was typically possible to free the Ulnar nerve for 20 mm and the Median nerve for 15-20 mm. Cuffs were installed as described for the distal nerve branches.

**Other implanted devices:** One pair of intramuscular EMG electrodes were installed in the Palmaris Longus muscle. A ground wire and a thermistor (YSI 44004) were implanted in the vicinity of the proximal cuffs. These devices were described by Hoffer (1990).

## C. Data Collection

During the third quarter, we continued with periodic recordings from all 8 cats of the first series using the protocol described in Progress Report #2. The recorded data are being analyzed to monitor long-term changes in compound action potentials, nerve cuff impedances, and nerve cuff integrity over a 6-month period (Objective 4c). The current status of each of the 8 cats is presented below (Table 3).

**TABLE 3. Status of implanted cats as of 31 August 1993**

Subject	Implant Date	Days implanted (as of Aug. 31)	Status
NIH 1, Dawson	May 10, 1993	101	Terminated on Aug. 19, 1993 Ulnar - cuffs removed after 7 days Median - several cuff leads broken
NIH 2, Pierre	May 19, 1993	104	Ulnar - data OK Median - data OK
NIH 3, Russell	June 2, 1993	90	Ulnar - data OK Median - data OK
NIH 4, Tristan	June 9, 1993	83	Ulnar - data OK Median - decline in signal amplitudes and then wires broke after day 75
NIH 5, Oliver	July 7, 1993	55	Ulnar - data OK Median - data OK
NIH 6, Victor	July 14, 1993	48	Ulnar - data OK Median - data OK
NIH 7, Samson	July 21, 1993	41	Ulnar - data OK Median - data OK
NIH 8, Winnie	Aug. 24, 1993	7	Ulnar - data OK Median - data OK

The first cat in the series was terminated prematurely, at 101 days, because of evident device failure. The neural signals on the Ulnar nerve declined markedly in the first week; the Ulnar nerve cuffs were removed 7 days after implantation. The neural signals on the Median nerve declined gradually, to the point that signals were no longer distinguishable. Post mortem examination showed that the recording electrodes had pulled out from both cuffs on the Median nerve, making stimulation and recording impossible. The short lead wire lengths used in the first cat (50 cm) and inadequate strain relief were suspected to be the causes for device failure in this subject. Starting with the second cat and in all subsequent cats, the implanted cuffs had 70 cm long leads, coiled generously for strain relief.

## D. Forelimb task paradigm: conceptual design and development

We are developing a forelimb reaching task designed to elicit voluntary movements by the subjects. The paradigm is based on a method used by Dr. Kris Horn and collaborators at the Barrow Neurological Institute in Phoenix, AZ to study cat forelimb reaching movements during cerebellar recordings (pers. comm.). In our research, we wish to study the natural use of the forelimb musculature during voluntary reaching and manipulations, and the patterns of sensory nerve activity that are recorded during such tasks. Reflex and voluntary responses to unexpected perturbations of joystick position or compliance will also be studied in detail. At later stages, we plan to combine sensory nerve recordings with FES of appropriate muscles.

The cats will be trained to, upon hearing a stimulus tone, reach out and pull a joystick in anticipation of a food reward. The joystick drive system will provide an adjustable resistance to the subject's pull. Food rewards will be given on successful completion of the task.

A quick, simple model of the joystick has been constructed and tested. The subjects took to the task very quickly. An unpowered model was built which includes the food reward system. Training of subjects will begin in the fourth quarter.

Implementation of the forelimb task consists of three main subsystems:

### 1) A joystick and electromechanical system to move it:

The joystick is a hollow tube with one end fixed and the other free to move in two horizontal directions (range= approximately 15 cm).

Two DC servo motors (PMI JR16M4CH) will provide motion in the two directions and allow the generation of 0 to 10 newtons of force at the end of the joystick.

Two switching servo amplifiers (SSA 75-10-30 or AXA 180-10-30) will drive these motors and allow for the possibility of very fast and accurate movements. The 30 Amp peak currents that these amplifiers are capable of will allow the generation of 2 cm perturbations in times of less than 10 milliseconds.

Transducers will measure force on the joystick and position in two directions. The servo motors will be equipped with tachometers for measuring velocity for monitoring and control purposes.

The joystick and motor mounting system will be constructed in the SFU Faculty of Science machine shop. Quotations for the servo motors and amplifiers are being evaluated now.

### 2) A pneumatic system to deliver a food reward:

The system is based on the system developed at the Barrow Neurological Institute. Semi-liquid food in a pressurized container is allowed to flow into a cap on the joystick when a reward is desired. The flow is pneumatically controlled (to allow the remote placement of the electrically noisy control solenoids). This system has been prototyped on our training model and seems to work well.

### 3) Software and a computer to provide control of the above systems:

The software will be written in C using an existing generic menu system. The setup portion of the program will allow the experimenter to specify all parameters related to the generation of motion or response to motion of the joystick, as well as the timing of intertrial intervals, the stimulus tone and the reward. The control portion of the program will continuously monitor all the parameters and make adjustments in real time. The control program will also trigger data acquisition on another computer at the appropriate times. Any unanticipated control problems will be modeled with a commercial software package (Simulink by Mathworks).

## V. Progress of Subcontractors in the Third Quarter

In the third quarter, our collaborations with the two subcontractors for this project, Dr. Dejan Popovic from U. Miami/U. Alberta and Dr. Jerry Loeb from Queen's U., was directed towards refinement of new approaches to construct self-spiraling electrodes. In the past six months, the Queen's group have accumulated a fairly large number of different materials, component designs, mechanical arrangements and fabrication procedures. These have been combined into a rather large number of different possible designs. Experience in such incremental development processes has shown that one can easily get lost in the details and overlook the basic principles that lead to discovering optimal, as opposed to barely adequate, designs. Dr. Loeb presents here his reanalysis of the problem based upon this experience.

### Design Principles

1. In order to record the highest level of signal from a nerve inside the cuff electrode, it is necessary that the nerve be confined in a closely fitting cylindrical space with non-conductive walls and a length about three times the space constant of the axons.
2. In order to exclude extrinsic signals from sources such as muscle outside of the cuff electrode, it is necessary to distribute tripolar contacts that are equidistant from each other within a close-fitting space that is uniform in cross-sectional area along its length and that has no breaks along its side-walls.
3. Connective tissue will always cover all exposed surfaces of a biocompatible foreign body and will track along surfaces until it meets more connective tissue.
4. If no provision is made to accomodate the additional volume of this connective tissue and some post-operative edema in the enclosed space, the pressure will cut off the blood supply and kill the nerve.
5. Biocompatibility of a material has two components: i) chemical - the material must not release toxic ions or compounds into the surrounding fluid or tissue; 2) mechanical - the material must not present textures or edges that will cut adjacent tissue or excessive bulk or stiffness that will crush it.
6. Any device that must be installed on delicate, relatively inaccessible structures by a surgeon under sterile operating conditions must be simple to manipulate and fool-proof to install correctly.
7. Any device that is expected to be produced commercially must be reliably manufacturable using simple, robust and repeatable procedures.

## Analysis of Design Problems

In the light of the above principles, the self-wrapping spiral nerve cuff presents several difficulties:

1. The spiral shape is a particular problem because it is unlikely to produce a perfect, long-term seal along the longitudinal entry seam without use of intraoperative adhesives (Principle 2) and such adhesives defeat the ability to self-adjust size post-operatively to accomodate swelling and connective tissue (Principle 4).
2. Even if the polymeric surfaces of the spiral tend to spring toward each other, the closing pressure will not exclude connective tissue, which will insinuate itself along the wedge-shaped junction until it forms a bridge to the outside and then gradually thicken that bridge to defeat the electrical principle of the sealed cylindrical space (Principle 3).
3. The self-wrapping concept is also a problem because the prestressed-lamination process required to achieve it inevitably adds bulk to the walls (Principle 5). It is also difficult to control during fabrication (Principle 7) to produce the correct amount of curl circumferentially without longitudinal ripples and bulges that defeat Principle 2.
4. A spiral with a relatively large, tightly sprung overlap is difficult to open and to apply intraoperatively (Principle 6).
5. The photolithographically produced electrode pattern is useful for achieving Principle 2 and avoids the danger of protruding strands posed by wire electrodes in the cuff (Principle 5), but substrate materials with suitable tensile and adhesive properties to support the thin film metallization tend to be hard materials that form sharp, traumatic edges that must not be exposed to tissue (Principle 5).

With these principles and problems in mind, the Queen's group is now working with the new photolithographic substrate supplied by Patrick van der Puije at Carleton University, in which a "universal" electrode pattern with five long contacts on very thin polyesterimide can be cut down into any shorter or narrower version required. In the next quarter, they will implant several cuffs on cat sciatic nerves (3 mm nominal diameter) and superficial peroneal and sural cutaneous nerves (1 mm nominal diameter). They will be used for stimulation and recording in freely moving animals for periods of 1-2 weeks and the cuff electrodes and adjacent nerves and connective tissues will be examined for biocompatibility. Incremental design changes will be made as needed and these cuffs will be produced in sizes and quantities as required for the scheduled chronic animal tests in Year 2 at Simon Fraser University.

## VI. Plans for Next Quarter

In the fourth quarter we intend to:

1. continue monitoring the status of implanted nerves and electrodes for a total of 6 months per cat
2. develop a post mortem and histopathological examination protocol for first year subjects
3. train cats on the forelimb reaching task and start recording data during this task
4. complete the construction of hardware for the reaching task
5. continue to collaborate on the bench evaluation of electrodes provided by Queen's University.

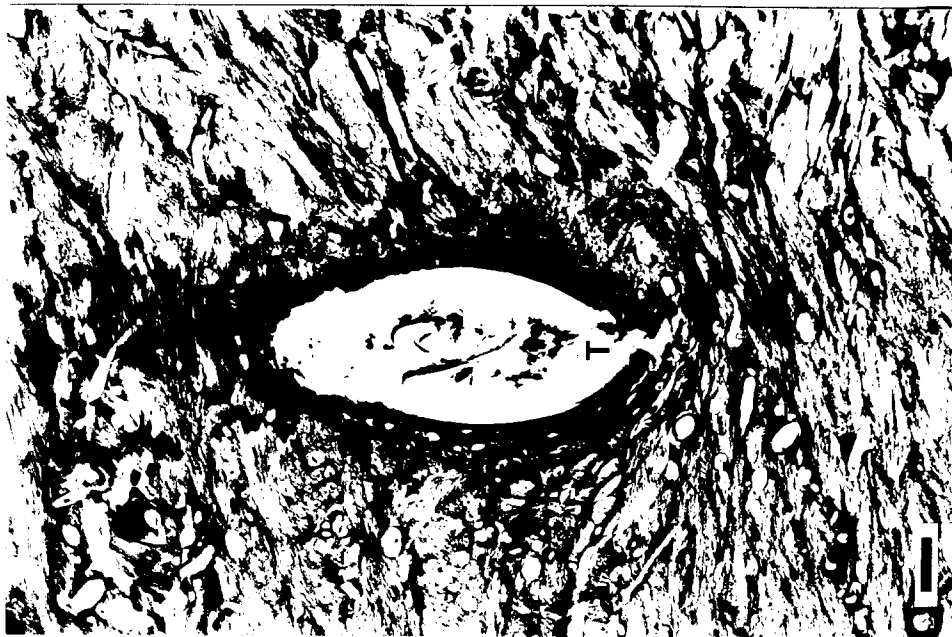


Figure 9A



Figure 9B



Figure 9C